

## Remarks

### The Amendments

Claim 7 has been rewritten to recite the characteristics of the isolated and purified TFPI in a wherein clause following the process steps in place of the preamble.

The preamble of claim 7 has also been amended for clarification to recite that the TFPI is “made by a method comprising” the process steps.

Claim 7 has also been amended at the step of transforming to recite that the second nucleotide sequence encodes a second protein, rather than ubiquitin. This amendment is supported by the specification which discloses, “The DNA encoding the factor VIIa/TF/Xa binding protein may be immediately preceded in frame by a second nucleotide sequence.” (Page 3, lines 24-26.) Ubiquitin is recited in new dependent claim 13. New claim 14 recites that the second protein is superoxide dismutase, which is supported at page 6, lines 14-16: “For example, the yeast superoxide dismutase (SOD) gene, can be linked at the 5’ terminus of the TFPI gene and the resulting fusion protein expressed in yeast.”

Claim 7 has also been amended at the step of incubating to recite that “the fusion protein is produced and cleaved to produce TFPI.” This amendment is supported by the specification which discloses that “the fusion peptide [is] capable of being cleaved within the yeast cells to produce authentic factor VIIa/TF/Xa binding protein.” (Page 3, lines 26-28.)

New claim 12 recites that the yeast cell from which the TFPI is isolated and purified is a *Saccharomyces cerevisiae* cell having a genome selected from the group consisting of VH6, AB122, and JSC310. New claim 12 is supported by the specification which discloses, “The yeast cells may be from the genus *Saccharomyces*, particularly *Saccharomyces cerevisiae* and

may have a genotype selected from the group consisting of: VH6, AB122, and JSC310.” (Page 3, line 28 to page 4, line 2.)

None of these amendments introduces new matter.

The Rejection of Claim 7 Under 35 U.S.C. § 112, Second Paragraph

Claim 7 has been rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully traverse. The Office Action lists two issues regarding the clarity of claim 7.

First, the Office Action notes that there appears to be a word or words missing in the preamble to link “TFPI” and “according.” (Paper 12, page 2, lines 12-14.) Claim 7 has been amended to recite “Isolated and purified TFPI made by a method comprising.”

Second, the Office Action notes that the recited method steps produce a ubiquitin-TFPI fusion protein rather than TFPI, as recited in the preamble. (Paper 12, page 2, lines 16-18.) Claim 7 has been amended to recite that yeast cells are incubated under conditions in which “the fusion protein is produced and cleaved to form TFPI and the second protein.” Thus it is clear that TFPI and not a TFPI fusion protein is purified from yeast.

Withdrawal of these rejections to claim 7 is respectfully requested.

The Rejection of Claim 7 Under 35 U.S.C. § 102(b)

Claim 7 is rejected under 35 U.S.C. § 102(b) as being anticipated by Wun *et al.* (*Thrombosis and Haemostasis* 68(1):54-59) or Nordfang *et al.* (*Biochemistry* 30(43):10371-10376). Applicants respectfully traverse.

To reject a claim as anticipated, a reference must teach exactly the same invention as is recited in a claim. “The identical invention must be shown in as complete detail as is contained in the . . . claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

Wun and Nordfang are cited as teaching TFPI expressed in and purified from mammalian cells and having activity similar to the TFPI of claim 7. (Paper 12, page 3, lines 13-16.) The Office Action asserts that, absent evidence to the contrary, the TFPI taught by Wun and Nordfang appears to be identical to the TFPI of claim 7. (Paper 12, page 4, lines 3-4.)

Claim 7 recites TFPI isolated and purified from yeast cells. TFPI purified from yeast cells as recited in claim 7 differs from TFPI purified from mammalian cells as taught by Wun and Nordfang because yeast and mammalian cells glycosylate proteins differently.

Yeast cells hypermannosylate proteins. Hypermannosylation is the attachment of a large number of mannose residues to a core oligosaccharide that has been added to a protein at a glycosylation consensus site. Jenkins *et al.* (*Nature Biotechnology* 14, 975-981, 1996; Appendix A) teaches that yeast cells hypermannosylate proteins by “the addition of a large number of mannose residues to the core oligosaccharide.” (Page 975, column 2, lines 22-23.) TFPI contains at least three amino acid glycosylation consensus sites at which a core oligosaccharide can be attached and subsequent hypermannosylated. “The primary sequence [of TFPI] also contains three Asn-X-Ser/Thr N-linked glycosylation consensus sites, the asparagine residues located at positions 145, 195, and 256.” (Specification at page 1, lines 22-24.) Thus TFPI isolated and purified from yeast cells is hypermannosylated.

Mammalian cells do not hypermannosylate proteins. See Jenkins *et al.* at page 976, Table 1. Thus, TFPI isolated and purified from mammalian cells is not hypermannosylated.

The isolated and purified TFPI recited of claim 7 is hypermannosylated while the TFPI isolated and purified by Wun and Nordfang is not. Thus the TFPI recited in claim 7 is not identical to the TFPI taught by either Wun or Nordfang. Wun and Nordfang do not anticipate claim 7.

Withdrawal of this rejection to claim 7 is respectfully requested.

Respectfully submitted,

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